

We claim:

Sub 2

1. A method of inhibiting neoplastic cellular proliferation and/or transformation of a mammalian breast or ovarian cell, comprising:

delivering to a mammalian breast or ovarian cell that overexpresses *PTTG*, a composition comprising a *PTTG* carboxy-terminal-related polynucleotide, said polynucleotide being complexed with a cellular uptake-enhancing agent, in an amount and under conditions sufficient to allow the polynucleotide to enter the cell, whereby neoplastic cellular proliferation and/or transformation of the cell is inhibited.

2. The method of Claim 1, wherein the cell is of human origin.

3. The method of Claim 1, wherein the cell exhibits neoplastic, hyperplastic, cytologically dysplastic, or premalignant cellular growth or proliferation.

4. The method of Claim 1, wherein the cell is a malignant cell.

5. The method of Claim 1, wherein the composition is delivered to the cell in vitro.

6. The method of Claim 1, further comprising administering the composition to a mammalian subject, such that the composition is delivered to the cell in vivo.

Sub 37

7. The method of Claim 1, wherein the polynucleotide is a DNA or DNA analog.

~~8. The method of Claim 1, wherein the polynucleotide is an antisense oligonucleotide.~~

Sub a3

~~9. The method of Claim 1, wherein the polynucleotide is a protein nucleic acid.~~

10. The method of Claim 7, wherein the composition further comprises an expression vector comprising a promoter, and the *PTTG* carboxy-terminal-related polynucleotide is operatively linked to the promoter in a transcriptional unit.

11. The method of Claim 10, wherein the polynucleotide encodes a *PTTG* carboxy-terminal peptide.

12. The method of Claim 11, wherein the polynucleotide defines a nucleotide base sequence encoding a mammalian PTTG-C peptide selected from the group consisting of

(A) peptides having an amino acid sequence of (SEQ. ID. NO.:9), (SEQ. ID. NO.:16), or (SEQ. ID. NO.:17);

5 (B) mammalian PTTG-C peptides having at least about 60% sequence homology with any of (A); and

(C) peptide fragments of (A) or (B) that comprise at least 15 contiguous amino acid residues and that function to downregulate endogenous *PTTG* expression and/or PTTG function.

13. The method of Claim 12, wherein the peptide fragment of (C) comprises a proline-rich region.

54624 14. The method of Claim 12, wherein the polynucleotide has a nucleotide sequence consisting of

(A) (SEQ. ID. NO.:10), (SEQ. ID. NO.:18), or (SEQ. ID. NO.:19)

(B) a degenerate coding sequence of any of (A);

5 (C) a sequence complementary to any of (A) or (B); or

(D) a polynucleotide fragment comprising at least 45 contiguous nucleotides of any of (A), (B) or (C).

15. A method of inhibiting neoplastic cellular proliferation and/or transformation of a mammalian breast or ovarian cell comprising:

delivering to a mammalian breast or ovarian cell that overexpresses PTTG, a composition comprising an expression vector comprising a promoter and a polynucleotide, said polynucleotide comprising a first DNA segment encoding a mammalian PTTG-C peptide, said polynucleotide being operatively linked to the promoter in a transcriptional unit, said PTTG-C peptide being selected from the group consisting of

(A) peptides having an amino acid sequence of (SEQ. ID. NO.:9), (SEQ. ID. NO.:16), or (SEQ. ID. NO.:17);

10 (B) mammalian PTTG-C peptides having at least about 60% sequence homology with any of (A); and

(C) peptide fragments of (A) or (B) that comprise at least 15 contiguous amino acid residues and that function to downregulate endogenous *PTTG* expression and/or PTTG function,

said expression vector being complexed with a cellular uptake-enhancing agent, in an amount and under conditions sufficient to enter the cell, such that the PTTG-C peptide is expressed in the cell, whereby  
 15 neoplastic cellular proliferation and/or transformation of the cell is inhibited.

16. The method of Claim 15, wherein the peptide fragment of (C) comprises a proline-rich region.

17. The method of Claim 15, wherein the polynucleotide further comprises a second DNA segment encoding an uptake-enhancing and/or importation-competent peptide segment.

18. The method of Claim 17, wherein the cellular uptake-enhancing and/or importation-competent polypeptide is a human immunodeficiency virus TAT-derived peptide segment or a signal peptide from Kaposi fibroblast growth factor.

19. The method of Claim 15, wherein the cell is of human origin.

20. The method of Claim 15, wherein the cell exhibits neoplastic, hyperplastic, cytologically dysplastic, or premalignant cellular growth or proliferation.

21. The method of Claim 15, wherein the cell is a malignant cell.

22. The method of Claim 15, wherein the composition is delivered to the cell in vitro.

23. The method of Claim 15, further comprising administering the composition to a mammalian subject in need of treatment, such that the expression vector is delivered to the cell in vivo.

24. A method of inhibiting neoplastic cellular proliferation and/or transformation of a mammalian breast or ovarian cell comprising:

delivering to a mammalian breast or ovarian cell a composition comprising a PTTG carboxy terminal peptide, or a biologically functional fragment thereof, complexed with a cellular uptake-enhancing agent, in an amount and under conditions sufficient to enter the cell whereby neoplastic cellular proliferation and/or transformation of the cell is inhibited.

5

25. The method of Claim 24, wherein the cell is of human origin.
26. The method of Claim 24, wherein the cell exhibits neoplastic, hyperplastic, cytologically dysplastic, or premalignant cellular growth or proliferation.
27. The method of Claim 24, wherein the cell is a malignant cell.
28. The method of Claim 24, wherein the composition is delivered to the cell in vitro.
29. The method of Claim 24, further comprising administering the composition to a mammalian subject, such that the polynucleotide is delivered to the cell in vivo.
30. The method of Claim 24, wherein said uptake-enhancing agent is a polycationic lipid agent.
31. The method of Claim 24, wherein said uptake enhancing agent comprises a cellular uptake-enhancing and/or importation-competent peptide segment.
32. The method of Claim 31, wherein the cellular uptake-enhancing and/or importation-competent peptide segment is a human immunodeficiency virus TAT-derived peptide segment or a signal peptide from Kaposi fibroblast growth factor.
33. A method of inhibiting neoplastic cellular proliferation and/or transformation of a human breast or ovarian cell, comprising:  
delivering to a human breast or ovarian cell a composition comprising a PTTG-C peptide being selected from the group consisting of
- 5 (A) peptides having an amino acid sequence of (SEQ. ID. NO.:9), (SEQ. ID. NO.:16), or (SEQ. ID. NO.:17);
- (B) mammalian PTTG-C peptides having at least about 60% sequence homology with any of (A); and
- (C) peptide fragments of (A) or (B) that comprise at least 15 contiguous amino acid residues
- 10 and that function to downregulate endogenous *PTTG* expression and/or PTTG function,

said expression vector being complexed with a cellular uptake-enhancing agent, in an amount and under conditions sufficient to enter the cell, such that the PTTG-C peptide is expressed in the breast or ovarian cell, whereby neoplastic cellular proliferation and/or transformation of the cell is inhibited.

34. The method of Claim 33, wherein the peptide fragment of (C) comprises a proline-rich region.

35. The method of Claim 33, wherein the cell exhibits neoplastic, hyperplastic, cytologically dysplastic, or premalignant cellular growth or proliferation.

36. The method of Claim 33, wherein the cell is a malignant cell.

37. The method of Claim 33, wherein the composition is delivered to the cell in vitro.

38. The method of Claim 33, further comprising administering the composition to a human subject in need of treatment, such that the PTTG-C peptide is delivered to the cell in vivo.

39. The method of Claim 33, wherein said uptake enhancing agent comprises a polycationic lipid.

40. The method of Claim 33, wherein said uptake enhancing agent comprises a cellular uptake-enhancing and/or importation-competent peptide segment.

41. The method of Claim 40, wherein the cellular uptake-enhancing and/or importation-competent peptide segment is a human immunodeficiency virus TAT-derived peptide segment or a signal peptide from Kaposi fibroblast growth factor.

42. The method of Claim 1, further comprising administering a cytotoxic chemotherapeutic agent to the cell simultaneously with or after delivering to the mammalian breast or ovarian the composition comprising the PTTG carboxy-terminal-related polynucleotide.

43. The method of Claim 15, further comprising administering a cytotoxic chemotherapeutic

agent to the cell simultaneously with or after delivering to the breast or ovarian cell the composition comprising the expression vector.

44. The method of Claim 24, further comprising administering a cytotoxic chemotherapeutic agent to the cell simultaneously with or after delivering to the mammalian breast or ovarian cell the composition comprising the PTTG carboxy terminal peptide or the biologically functional fragment thereof.

45. The method of Claim 33, further comprising administering a cytotoxic chemotherapeutic agent to the cell simultaneously with or after delivering to the human breast or ovarian cell the composition comprising the PTTG-C peptide.

sub 25 46. The method of Claim 42, wherein the cytotoxic chemotherapeutic agent is selected from the group essentially consisting of paclitaxel, 5-fluorouracil, cisplatin, carboplatin, methotrexate, daunorubicin, doxorubicin, vincristine, vinblastine, busulfan, chlorambucil, cyclophosphamide, melphalan, and ethyl ethanesulfonic acid.

47. The method of Claim 43, wherein the cytotoxic chemotherapeutic agent is selected from the group essentially consisting of paclitaxel, 5-fluorouracil, cisplatin, carboplatin, methotrexate, daunorubicin, doxorubicin, vincristine, vinblastine, busulfan, chlorambucil, cyclophosphamide, melphalan, and ethyl ethanesulfonic acid.

48. The method of Claim 44, wherein the cytotoxic chemotherapeutic agent is selected from the group essentially consisting of paclitaxel, 5-fluorouracil, cisplatin, carboplatin, methotrexate, daunorubicin, doxorubicin, vincristine, vinblastine, busulfan, chlorambucil, cyclophosphamide, melphalan, and ethyl ethanesulfonic acid.

49. The method of Claim 45, wherein the cytotoxic chemotherapeutic agent is selected from the group essentially consisting of paclitaxel, 5-fluorouracil, cisplatin, carboplatin, methotrexate, daunorubicin, doxorubicin, vincristine, vinblastine, busulfan, chlorambucil, cyclophosphamide, melphalan, and ethyl ethanesulfonic acid.

add  
B-11